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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,819	01/30/2001	Kathleen E. Rodgers	98,365-B1	3008

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EXAMINER

AUDET, MAURY A

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/772,819

Applicant(s)

RODGERS ET AL.

Examiner

Maury Audet

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49-54, 57-62, 65 and 66 is/are pending in the application.
- 4a) Of the above claim(s) 55, 56, 63 and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 49-54, 57-62, 65 and 66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Claims 1-48 were previously cancelled and new claims 49-66 added. Claims 55-56 and 63-64 have been cancelled. Claims 49-54, 57-62, and 65-66 are pending.

Election/Restrictions

Applicant's election with traverse of Group 17 and SEQ ID NO: 18, as the invention (drawn to claims 49-54, 57-62, and 65-66), filed September 29, 2003, is acknowledged. The traversal is on the ground(s) that "each of the other polypeptides has overlapping amino acid sequences with the elected species". This is not found persuasive. For instance, elected SEQ ID NO: 18 has the following 7-mer sequence: RVYAHPPF. The next sequence, SEQ ID NO: 19 has the following 8-mer sequence: DRVTVHPF. In a comparison of merely these two sequences, three residues 1-3 and 5-7 of SEQ ID NO: 18 do overlap with residues 2-4 and 6-8 of SEQ ID NO: 19. However, the substitution of Val in residue 5 of SEQ ID NO: 19, for the Ala of residue 4 of SEQ ID NO: 18, makes each sequence distinct, *lacking a substantial core structure*; and thus requiring separate sequence/compound searches. Therefore, the overlapping of a mere three sequences in a short 7 or 8-mer peptide, does not confer a substantial enough "core" structure which would allow "a search using common amino acid sequences", which Applicant argues. Furthermore, this would NOT "identify any relevant references for larger groups of polypeptides". With regard to any related applications, "It is well settled that whether similar claims have been allowed to others is immaterial." *In re Giolito*, 530 F.2d 397, 188 USPQ 645 (1976). Each application, even if containing related subject matter, must be searched anew and examined on its own merits.

Art Unit: 1654

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112 1st Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-54, 57-62, and 65-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a “written description” rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 “Written Description” Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the “written description” inquiry, is *whatever is now claimed*” (see page 1117).

The claimed invention, and claims 49-54, 57-62, and 65-66, is drawn to a method for treating (or preventing) a bone disorder or a bone disorder that results in weakened bones, comprising administration of elected SEQ ID NO: 18.

Art Unit: 1654

One of skill in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (see *Vas-Cath* at page 1116). Namely, although the specification at page 36-37 describe that SEQ ID NOS: 1, 4, and 45 (although not elected SEQ ID NO: 18), may be useful (only 50% were observed with new bone growth, the study was only conducted on rats, and the study does not indicate how many subjects were tested), as a therapeutic agent for “bone healing” and the formation of new bone; *SEQ ID NO: 18 has not been tested*.

Thus, neither the claims nor the specification details whether SEQ ID NO: 18 would be able to stimulate bone growth and thus treat a bone disorder or a bone disorder that results in weakened bone. Rather, only that some portion of SEQ ID NOS: 1, 4, and 45 may be to stimulate new bone growth. With the substantial variability among the broad genus of peptides, including SEQ ID NO: 18, due to their short length, it is not clear as whether SEQ ID NO: 18 could carry out the invention’s method, even if it is shown to be similar to, in some residues, to one of the enabled SEQ ID NOS: 1, 4, or 45. One of skill in the art would not recognize from the disclosure that the Applicant was in possession of the invention, namely the use of SEQ ID NO: 18 (or any other of the peptides) to stimulate bone growth and thus treat a bone disorder or a bone disorder that results in weakened bone.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Art Unit: 1654

Claim Rejections - 35 USC § 112 1st Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-54, 57-62, and 65-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988)). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the use of peptide SEQ ID

NOS: 18, in a method to stimulate bone growth and thus treat a bone disorder or a bone disorder that results in weakened bone, for the following reasons:

Art Unit: 1654

The nature of the invention: drawn to a method for treating (or preventing) a bone disorder or a bone disorder that results in weakened bones, comprising administration of elected SEQ ID NO: 18.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that a single amino acid substitutions can alter the antigen-binding specificity of peptides, and thus alter peptide function either in vitro or in vivo (i.e. “in a subject”) (Rudikoff et al., Proc Natl Acad Sci U S A. 1982 Mar;79(6):1979-83, page 1979, and page 1982, 1st s. under “Implications for Generation of Diversity”).

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification does not teach the testing or capability of SEQ ID NO: 18, as a method for treating (or preventing) a bone disorder or a bone disorder that results in weakened bones. Rather, only that some portion of SEQ ID NOS: 1, 4, and 45 (the only peptides tested) may be to stimulate new bone growth. Furthermore, only 50% new bone growth was evidenced, and only in part by (or in whole of one or part of another) of SEQ ID NO: 1, 4, and 45; it is unclear whether SEQ ID NO: 18 (or any other of the peptides) would be able to stimulate bone growth and thus treat a bone disorder or a bone disorder that results in weakened bones. The tests were only conducted on rats, and the study does not indicate how many subjects were tested.

The specification has not defined how it is known that these derivative peptides are capable of modulating such activity “in a subject”.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn to elected SEQ ID NO: 18. As described above, with the substantial variability among the broad genus of peptides, including SEQ ID NO: 18, due to their short length and the lack of reliability of the testing and results, it is not clear as whether SEQ ID NO: 18 could carry out the invention's method, even if it is shown to be similar to, in some residues, to one of the enabled SEQ ID NOS: 1, 4, or 45. As Rudikoff et al. teach, a single amino acid substitution may be enough to alter peptide specificity or function. Absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art; namely as to how it is known that SEQ ID NO: 18 would be able to stimulate bone growth and thus treat a bone disorder or a bone disorder that results in weakened bones, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112 1st Scope

Claims 49-54, 57-62, and 65-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while it may be enabling for treating and/or reducing the risk of a bone disorder or a bone disorder that results in weakened bones, does not reasonably provide enablement for preventing any bone disorder or any bone disorder that results in weakened bones using such a composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants have reasonably demonstrated/disclosed that SEQ ID NOS: 1, 4, and 45 (although not elected SEQ ID NO: 18), may be useful (only 50% were observed with new bone growth, the study was only conducted on rats, and the study does not indicate how many subjects

Art Unit: 1654

were tested), as a therapeutic agent for "bone healing" and the formation of new bone and/or reducing the risk of bone disorders (specification page. 36-37). However, the claims also encompass using the claimed peptides to prevent any bone disorder or any bone disorder that results in weakened bones which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does the term "treat", especially with respect to preventing type II diabetes (which, is not recognized in the medical art as being a totally preventable condition).

Accordingly, it would take undue experimentation without a reasonable expectation of success for one of skill in the art to make and/or use the claimed composition which would function to prevent any bone disorder or any bone disorder that results in weakened bones.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-54, 57-62, and 65-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 49-54, 57-62, and 65-66, the invention is unclear since, as claimed, it is drawn to the use of a sequence of at least three contiguous amino acids, many alternatives, including sequences, thereof, and elected SEQ ID NO: 18. In response to this action, it is suggested that Applicant amend the claims to be drawn to elected SEQ ID NO: 18.

In claim 49, it is unclear what is contemplated as “a bone disorder that results in weakened bones”. Specification page 3-4 describes that “[a]mong pathological conditions associated with abnormal bone cell function are osteoporosis . . . age-related loss of bone mass” and 7 general other disorders in-between. It is assumed that pathological conditions refers to “bone disorders that result in weakened bones”; however, it is not clear whether all these diseases actually cause weakened bones (the disorder targeted by the invention). Since the specific diseases which may be treated is unclear based on the claims, it is suggested that Applicant specifically claim those diseases which are “bone disorders that result in weakened bones”.

In claim 49, is unclear what the invention really is due to the confusing language “treating . . . *a bone disorder that results in weakened bone*, comprising the administration of an amount effective for treating or preventing *a bone disorder* . . .”. Applicant begins with a narrower treating of “a bone disorder that results in weakened bones” to the broader “a bone disorder”. It is suggested that, as described in the 1st 112 2nd above, Applicant 1st specifically recite those disorders that result in weakened bones, and then in the 2nd instance identify antecedent basis by claiming “*the* bone disorder” rather than “a bone disorder.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 49-54, 57-62, and 65-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,248,587 B1 (Rodgers et al.). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Rodgers et al. '587 teach a method accelerating the proliferation of mesenchymal stem comprising contacting the mesenchymal stem cells (MSC) (claim 1) with Applicants SEQ ID NO : 18 (claim 2). It is well known in the art that MSC are pluripotent progenitor cells that possess the ability to differentiate into bone.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a bone disorder, and more specifically a bone disorder with weak bones, using the SEQ ID NO: 18 of Rodgers et al. '587, because Rodgers et al. '587 teach the use of SEQ ID NO: 18 to increase MSC's and thus bone growth; and because it is well known that the primary underlying etiology of weak bones is insufficient bone growth.

Claims 49-54, 57-62, and 65-66 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,498,138 (Rodgers et al.). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Rodgers et al. '138 teach a method for accelerating the production of a tissue equivalent comprising contacting the tissue equivalent with an amount effective to accelerate generation of tissue equivalents of Applicant's SEQ ID NO: 18 (RVY AHPF; see where R2-R8 of claim 1 may be). It is well known in the art that MSC are pluripotent progenitor cells that possess the ability to differentiate into bone.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a bone disorder, and more specifically a bone disorder with weak bones, using the SEQ ID NO: 18 of Rodgers et al. '138, because Rodgers et al. '138 teach the use of SEQ ID NO: 18 to increase the tissue MSC's and thus bone growth; and because it is well known that the primary underlying etiology of weak bones is insufficient bone growth.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
November 14, 2003



CHRISTOPHER R. TATE
PRIMARY EXAMINER